DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/29/2009 has been entered.

Claim(s) 15, 16, 18-20, 38, 41, 42, 52-54, 56-61, 69, and 72-74 are pending. Claims 15, 16, 18-20, 38, 41, 42, 52-54, 56-61, 69, and 72-74 are hereby examined on the merits.

Objections

Claims 42 is objected to as being dependent on a higher numbered claim

In Claim 15, 56, and 69, "the" needs to be inserted before "active site" in order to be properly understood.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15, 16, 18, 19, 20, 38, and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Tam et al, U.S. Patent 5,229,490.

The instantly claimed invention is drawn to a method of suppressing or inhibiting the processing of an antigen by an antigen presenting cell, the method comprising contacting the cell with an inhibitor of asparaginyl endopeptidase, wherein the inhibitor of asparaginyl endopeptidase is a competitive inhibitor comprising a peptide selected from the group consisting of Ala-Glu-Asn-Lys-NH (AENK) (SEQ ID NO: 1) and Lys-Asn-Asn-Glu-NH (KNNE) (SEQ ID NO: 2).

Tam discloses the peptide Asn-**Ala-Glu-Asn-Lys**-Glu-Glu-Leu-Thr-Ser-Ser-Asp-Pro-Glu-Gly-Gln-Ile-Met, in Claim 14, where the SEQ ID NO:2 is contained within the sequence disclosed. The language of the claim is open, therefore, the amino acids on either side of SEQ ID NO:2 are permitted, especially in light of the fact that SEQ ID NO:2 does not terminate with an $-NH_2$. The sequence for SEQ ID NO:2 ends with an –NH, implying there must be another atom attached to be consistent with the valence of the nitrogen. Given that the peptides were administered, which meets the limitation of contacting the cell, the peptides would have functioned to suppress the processing of an antigen presenting cell, readable on Claims 41. Given the absence of a definition for blocking group, acetyl being the only one envisioned by Applicants, the flanking amino acid on the N-terminus, as well as the Gly-linker-Lys dendramer on the C-terminus serves as a blocking group, readable on Claims 16, 17, and 38. Further, at the time of the synthesis of the compounds, Merrifield protocols were used and blocking groups

were employed in the making of the peptide. Thus, prior to the released of the peptide from the resin, the peptide had a blocking group attached to the peptide, see materials and methods in the making of the product. Lastly, given the dependency of Claim 20 from Claim 15, the adjacent residues C-terminal to Asn must be Q and must be the group capable of reacting with the active site of asparaginyl endopeptidase. Therefore, the invention is anticipated by the prior art reference.

Claims 52, 53 and 69 are rejected under 35 U.S.C. 102(e) as being anticipated by Bojanovska et al, The preparation and metabolic fate of tritiated Nα-acetyl[2-O-methyltyroisine] Oxytocin", Collection of Czechoslovak Chemical Communications, (1974), 44(9), 2702-2709.

The instantly claimed invention is drawn to an inhibitor of asparaginyl endopeptidase which has the structure B1-(X_aX_n)Asn-Q wherein B1 is any suitable N terminal blocking group; X_aX_n are the n amino acid residues immediately N terminal to an Asn cleavage site in the invariant chain of Class II MHC molecules; Asn is an asparagine residue; and Q is a group capable of reacting with the active site of asparaginyl endopeptidase and forming a covalent complex therewith.

Bojanovska et al discloses L-isoleucyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-L-prolyl-(4→1')-disulfide with N-acetyl-L-cysteinyl-O-methyl-L-tyrosine L-Leucine, CAS Registry No: 72289-64-6P. The compound reads on BI-(X_aX_n)Asn-Q, where Q is the remaining portion of the molecule C-terminal to the Asn and is capable of reacting with

with the reactive site, and the molecule is protected with an Acetyl blocking group, i.e., it has the structure which is open language. The phrase "*amino acids residues immediately N-terminal to an Asn cleavage site in the invariant chain of Class II MHC molecules*" is simply taken as any of the 20 naturally occurring amino acids, because the claim language does not specify a specific sequence, only residues of such a sequence. Because the limitations of the claims are met, the functional properties are met, and would be inherent.

Claim 52-54, 61, 69 is rejected under 35 U.S.C. 102(b) as being anticipated by Mullner, et al, US 5,461,035.

The instant invention is drawn to an inhibitor which is any of B1-Ser-Gln- Asn-Q; B1-**Leu-Glu-Asn**-Q; B1-Leu-Gln-Asn-Q; B1-Pro-Glu-Asn-Q; B1-Leu-Lys-Asn-Q; B1-Gln- Ash-Q; B 1-Glu-Asn-Q; B 1-Asp-Glu-Asn-Q; B1-Asn-Gly-Asn-Q; B 1-Phe-Pro-Asn-Q; B 1-Val- Pro-Asn-Q; and B1-His-His-Asn-Q.

Mullner et al discloses the peptide Acetyl-**Leu-Glu-Asn**-Tyr-Cys-Asn-OH and pharmaceutical formulations (see claims of the US patent). This peptide is readable on the second peptide of the Markush group, that of peptide B1-**Leu-Glu-Asn**-Q supra. The sequence -Tyr-Cys-Asn-OH contained in the prior art disclosed peptide is Q, and is capable of reacting at the active site as claimed. Note that "capable of" does not mean it must react. Further, the B1 moiety is that of Acetyl, and is the protecting group. Because the peptide is antecedent to Claims 52 and 53, i.e., X_n is 2, and B1 is an acetyl

protecting group, Claims 52 and 53 are also rejected as being anticipated by the prior art peptide. Since the reference disclose Leu and Glu conjugated to Asn, this meets the limitation of claim 61. For claim 69, the presence Cys in the sequence meets the limitation of a group that is "capable of" reacting with active site cystine. This is because Cys can form a disulfide bridge with another Cys.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 16, 18-20, 38, 41, 42, 52-54, 56, 61, and 72-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 15, 38, and 56, the peptides end with an –NH. The meaning of this is unclear. In the instant case there is no indication of how the valence of the nitrogen is completed. Correction is required.

Because the dependent claims do not correct the meaning of –NH, they too must be rejected.

In Claim 52, 53, and 72, the "a" in Xa is not defined and is, therefore, indefinite. Dependent claims to Claim 52 are also indefinite as they do not correct the raised issue.

In Claim 54, the sequences lack antecedent basis to Claim 52. Claim 54 recites specific amino acids, and it is unclear to which these sequences belong, that of X_a or X_n.

Since the Claims to which it depends does appear to make a distinction, the specific sequences must relate to the Markush in a manner that clearly indicates which amino acids are part of the defined sequences.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 16, 18-20, 52-54, 56, 60, 61, 69, and 72-74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.
The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed.

The factors considered in the Written Description requirement are:

(1) level of skill and knowledge in the art,

(2) partial structure,

(3) physical and/or chemical properties,

(4) functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and

(5) the method of making the claimed invention.

In the instant case, the claims are drawn to an inhibitor of asparaginyl endopeptidase is a non-competitive inhibitor of asparaginyl endopeptidase which comprises an asparagine residue to which is attached a group capable of reacting with active site cysteine of asparaginyl endopeptidase and forming a covalent complex therewith, Claim 15. Claim 52 and 72 is further drawn to an inhibitor and its associated method for an asparaginyl endopeptidase which has the structure Bl-(X_aX_n)Asn-Q wherein B1 is any suitable N terminal blocking group; X_aX_n are the n amino acid residues immediately N terminal to an Asn cleavage site in the invariant chain of Class II MHC molecules; Ash is an asparagine residue; and Q is a group capable of reacting with the active site of asparaginyl endopeptidase and forming a covalent complex therewith. Lastly, Claim 69 is drawn to a pharmaceutical composition comprising a non-competitive inhibitor of asparaginyl endopeptidase which comprises an asparagine residue to which is attached a group capable of reacting with active site cysteine of asparaginyl endopeptidase and forming a covalent complex therewith, and a pharmaceutically acceptable carrier.

(1) Level of skill and knowledge in the art:

The level of skill to practice the art of the instantly claimed invention is high with regard to synthesis, isolation and purification, as well as bioassays, cell culture and in vitro work in the structure function studies needed to characterize the compounds to their intended use.

(2) Partial structure: (3) Physical and/or chemical properties: and (4) Functional characteristics:

The only partial structure to the instantly claimed invention is that of an Asn amino acid, clustered between a undescribed Q moiety and a “blocking group." All other components of the invention are described only in functional language.

(5) Method of making the claimed invention:

For the peptides, standard Merrifield synthesis, known to the skilled artisan.

As stated supra, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that Claim(s) 15, 20, 52, 53, 56, 69, and 72 are a broad generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of compound described or claimed in functional language, or claimed without a clear and precise core structure.

It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. "MPEP § 2163.

Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the

specification. While having written description for the compounds of Claim 38 or 54, there is insufficient description of a common core structure that would allow one of skill in the art to practice the invention as claimed. A "Q moiety that is capable of reacting" leaves what this functional group is to the imagination of the skilled artisan. The phrase, "*inhibitor of asparaginyl endopeptidase is a non-competitive inhibitor of asparaginyl endopeptidase which comprises an asparagine residue to which is attached a group capable of reacting with active site cysteine of asparaginyl endopeptidase and forming a covalent complex therewith*, is so broad as to nearly be indefinite and does not correlated the intended function to a common core structure other than a the amino acid Asn. It appears the Applicants have taken a few examples and expanded the species to a genus that is beyond the skill of artisan to know what structures are essential for the correlated function. B1-(XaXn)-Asn-Q is far from providing the necessary and requisite structural information. While amino acids are known, and Asn is specifically defined, B1 and Q are not described, nor is XaX_n as for most peptidases, specific sequences are normally required for the peptidase to recognize.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")

Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Prior art contained in the reference of record can be applied in the next office action.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas S. Heard whose telephone number is (571) 272-2064. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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